Set	Items	Description
S1	373	AU='MARGOLSKEE R' OR AU='MARGOLSKEE R F' OR AU='MARGOLSKEE R.' OR AU='MARGOLSKEE R.F.' OR AU='MARGOLSKEE RF' OR AU='MARGOLSKEE ROBERT' OR AU='MARGOLSKEE ROBERT F'
S2	120066	TASTE OR BITTER
S3	2129356	CALCIUM
S4	1065123	CHANNEL
S5	202	S1 AND S2
S6	28	S5 AND S4
S7	15	RD (unique items)
S8	2080	TRANSIENT(W)RECEPTOR(W)POTENTIAL
S9	11	S1 AND S8
S10	4	RD (unique items)
S11	15	S7 OR S10

11/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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15115185 22650589 PMID: 12765699
Making sense with TRP channels: store-operated calcium entry and the ion channel Trpm5 in taste receptor cells.
Perez Cristian A; **Margolskee Robert F** ; Kinnamon Sue C; Ogura Tatsuya
Department of Physiology & Biophysics, Howard Hughes Medical Institute, Mount Sinai School of Medicine, New York University, New York, NY 10029, USA. Cristian.Perez@rockefeller.edu
Cell calcium (Scotland) May-Jun 2003, 33 (5-6) p541-9, ISSN 0143-4160 Journal Code: 8006226
Contract/Grant No.: DC 00766; DC; NIDCD; DC 03055; DC; NIDCD; DC 03155; DC; NIDCD; DC 05140; DC; NIDCD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
The sense of **taste** plays a critical role in the life and nutritional status of organisms. During the last decade, several molecules involved in **taste** detection and transduction have been identified, providing a better understanding of the molecular physiology of **taste** receptor cells. However, a comprehensive catalogue of the **taste** receptor cell signaling machinery is still unavailable. We have recently described the occurrence of calcium signaling mechanisms in **taste** receptor cells via apparent store-operated channels and identified Trpm5, a novel candidate **taste** transduction element belonging to the mammalian family of **transient receptor potential** channels. Trpm5 is expressed in a tissue-restricted manner, with high levels in gustatory tissue. In **taste** cells, Trpm5 is co-expressed with **taste** -signaling molecules such as alpha-gustducin, Ggamma(13), phospholipase C beta(2) and inositol 1,4,5-trisphosphate receptor type III. Biophysical studies of Trpm5 heterologously expressed in Xenopus oocytes and mammalian CHO-K1 cells indicate that it functions as a store-operated **channel** that mediates capacitative calcium entry. The role of store-operated channels and Trpm5 in capacitative calcium entry in **taste** receptor cells in response to **bitter** compounds is discussed.

11/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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14915128 22571192 PMID: 12684446
Electrophysiological characterization of voltage-gated currents in defined taste cell types of mice.
Medler Kathryn F; **Margolskee Robert F** ; Kinnamon Sue C
Department of Biomedical Sciences, Colorado State University, Fort Collins, Colorado 80523, USA. Kathryn.Medler@colostate.edu
Journal of neuroscience - the official journal of the Society for Neuroscience (United States) Apr 1 2003, 23 (7) p2608-17, ISSN 1529-2401 Journal Code: 8102140
Contract/Grant No.: DC00244; DC; NIDCD; DC00766; DC; NIDCD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Despite extensive immunological characterization of the cells within **taste** buds, little is known about the functional significance of the different cell types. In this study, we use **taste** cells isolated from mouse vallate and foliate papillae to characterize voltage-gated currents in the three principal elongate types of **taste** cells: type I, II, and III. Cell types are identified by using antibodies to external epitopes [antigen H for type I cells, antigen A for type II cells, and neural cell adhesion molecule (NCAM) for type III cells]. In addition, we identify the subset of type II cells that contains alpha-gustducin, a G-protein involved

in **bitter** transduction, by using transgenic mice expressing green fluorescent protein under the control of the gustducin promoter. Our results indicate that antigen H-immunoreactive (-IR) cells and many of the antigen A-IR cells have small voltage-gated inward Na(+) and outward K(+) currents but no voltage-gated Ca(2+) currents. In contrast, a subset of antigen A-IR cells and all NCAM-IR cells have large inward Na(+) and outward K(+) currents as well as voltage-gated Ca(2+) currents. Unexpectedly, all gustducin-expressing cells lacked voltage-gated Ca(2+) currents, suggesting that these cells use mechanisms other than classical synapses to communicate signals to the brain.

11/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14115268 22292154 PMID: 12368808
A transient receptor potential channel **expressed in** taste **receptor cells.**
Perez Cristian A; Huang Liquan; Rong Minqing; Kozak J Ashot; Preuss Axel K; Zhang Hailin; Max Marianna; **Margolskee Robert F** ; et al
Howard Hughes Medical Institute, Mount Sinai School of Medicine, New York University, Box 1677, 1425 Madison Avenue, New York, New York 10029, USA.
Nature neuroscience (United States) Nov 2002, 5 (11) p1169-76, ISSN 1097-6256 Journal Code: 9809671
Contract/Grant No.: DC00310; DC; NIDCD; DC03055; DC; NIDCD; DC03155; DC; NIDCD; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We used differential screening of cDNAs from individual **taste** receptor cells to identify candidate **taste** transduction elements in mice. Among the differentially expressed clones, one encoded Trpm5, a member of the mammalian family of **transient receptor potential** (TRP) channels. We found Trpm5 to be expressed in a restricted manner, with particularly high levels in **taste** tissue. In **taste** cells, Trpm5 was coexpressed with **taste** -signaling molecules such as alpha-gustducin, Ggamma13, phospholipase C-beta2 (PLC-beta2) and inositol 1,4,5-trisphosphate receptor type III (IP3R3). Our heterologous expression studies of Trpm5 indicate that it functions as a cationic **channel** that is gated when internal calcium stores are depleted. Trpm5 may be responsible for capacitative calcium entry in **taste** receptor cells that respond to **bitter** and/or sweet compounds.

11/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11312397 98191707 PMID: 9518702
Extracellular K+ activates a K(+)- and H(+)-permeable conductance in frog taste **receptor cells.**
Kolesnikov S S; **Margolskee R F**
Howard Hughes Medical Institute, New York, NY, USA.
Journal of physiology (ENGLAND) Mar 1 1998, 507 (Pt 2) p415-32, ISSN 0022-3751 Journal Code: 0266262
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
1. The effect of extracellular K+ on membrane currents of bull frog (Rana catesbeiana) **taste** receptor cells (TRCs) was investigated by the patch clamp and fast perfusion techniques. Extracellular K+ (2.5-90 mM) increased a TRC resting conductance and enhanced both inward and outward whole-cell currents. 2. To isolate the inward current activated by external potassium

(PA current), TRCs were dialysed with 110 mM NMGCl while extracellular NaCl was replaced with NMGCl. Under these conditions, the PA current displayed an S-shaped current-voltage (I-V) curve in the -100 to 100 mV range. Extracellular Rb+ and NH4+, but not Li+, Na+ or Cs+, evoked similar currents. 3. The PA current reversal potential (Vr) did not follow the equilibrium K+ potential under experimental conditions. Therefore, K+ ions were not the only current carriers. The influence of other ions on the PA current Vr indicated that the channels involved are permeable to K+ and H+ and much less so to Na+, Ca2+ and Mg2+. Relative permeabilities were estimated on the basis of the Goldman-Hodgkin-Katz equation as follows: PH:PK:PNa = 4000:1:0.04. 4. All I-V curves of the PA current were nearly linear at low negative potentials. The slope conductance at these voltages was used to characterize the dependence of the PA current on external K+ and H+. The slope conductance versus K+ concentration was fitted by the Hill equation. The data yielded a half-maximal concentration, K1/2 = 19 +/- 3 mM and a Hill coefficient, nH = 1.53 +/- 0.36 (means +/- S.E.M.). 5. The dependence of the mean PA current and the current variance on the K+ concentration indicated a rise in the open probability of the corresponding channels as extracellular K+ was increased. With 110 mM KCl in the bath, the single **channel** conductance was estimated at about 6 pS. Taken together, the data suggest that extracellular K+ may serve as a ligand to activate specific small-conductance cation channels (PA channels). The mean number of the PA channels per TRC was estimated as at least 2000. 6. Extracellular Ba2+, Cd2+, Co2+, Ni2+ and Cs+ blocked the PA current in a potential-dependent manner. The PA current was blocked by Cs+ as quickly as the blocker could be applied (approximately 15 ms). The time course of the divalent cation block was well fitted by a single exponential function. The time constants were estimated at 26.5 +/- 1.9, 41.7 +/- 3.1, 56.1 +/- 4.2 and 370 +/- 18 ms at 1 mM Cd2+, Co2+, Ni2+ and Ba2+, respectively. The blocker efficiency at negative voltages followed the sequence: Cs+ > Cd2+ > Ba2+ > Ni2+ > Co2+. 7. The data indicate that protons and divalent blockers act within the PA **channel** pore and that H+ and the divalent ions probably act via similar mechanisms to affect the PA current. These observations and the strong pH dependence of the PA current Vr suggest that H+ occupation of the PA **channel** pore leading to interruption of K+ flux is the main mechanism of the pH dependence of the PA current. 8. Extracellular K+ enhanced the sensitivity of isolated TRCs to bath solution acidification due to activation of the PA channels. With 10 mM K+ in the bath, half-maximal depolarization of the TRCs was observed at pH values of 6.4-6.8. The possible role of the PA channels in sour transduction is discussed.

11/3,AB/5 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13881704 BIOSIS NO.: 200200510525
Insights into taste transduction and perception from molecular, biochemical and transgenic studies.
AUTHOR: **Margolskee Robert F** (a
AUTHOR ADDRESS: (a)Department of Physiology and Biophysics, Howard Hughes Medical Institute, Mount Sinai School of Medicine, 1425 Madison Avenue, Box 1677, New York, NY, 10029**USA
JOURNAL: Abstracts of Papers American Chemical Society 224 (1-2):pAGFD 16 2002
MEDIUM: print
CONFERENCE/MEETING: 224th National Meeting of the American Chemical Society Boston, MA, USA August 18-22, 2002
ISSN: 0065-7727
RECORD TYPE: Citation
LANGUAGE: English
2002

11/3,AB/6 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

13285282 BIOSIS NO.: 200100492431
Functional expression of TRP-T, a store operated calcium channel **expressed in** taste **cells.**
AUTHOR: Perez C A(a); Preuss A; Kozak J A; Huang L(a); Rong M(a); Max M; **Margolskee R F** (a
AUTHOR ADDRESS: (a)Howard Hughes Medical Institute, Mount Sinai School of Medicine, New York, NY**USA
JOURNAL: Society for Neuroscience Abstracts 27 (1):p755 2001
MEDIUM: print
CONFERENCE/MEETING: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: **Taste** receptor cells (TRCs) transduce responses to tastants using a diversity of mechanisms including ion channels (for sodium salts, acids, and fat **taste**) and G-protein coupled receptor (GPCR) cascades (for sugars, sweeteners, **bitter** and glutamate/umami compounds). During the past decade, a number of constituent elements from these GPCR cascades have been identified. Among those elements there are the T2R/TRB family of candidate receptors for **bitter** compounds, T1R3, a candidate receptor for sweet compounds, the G protein subunits alpha-gustducin, Gbeta3 and Ggamma13, and downstream elements such as PDE1A, PLCbeta2, and IP3 type III receptor (IP3R3). Nevertheless, additional downstream elements are expected to be present in TRCs. To better understand the transduction pathways in gustducin-positive TRCs we set out to identify genes preferentially expressed in gustducin-positive TRCs. Differential hybridization screenings led us to the cloning of TRP-T, a novel member of the Trp (**transient receptor potential**) family of ion channels. TRP-T co-expresses with alpha-gustducin, Gbeta3, Ggamma13, PLCbeta2 and IP3R3 in TRCs. Functional expression of TRP-T studied by electrophysiological and calcium imaging techniques demonstrated its ability to work as a store operated calcium **channel** , sensitive to inhibition by lanthanum. TRP-T is a putative effector present in the sweet and **bitter** transduction pathways of TRCs.

2001

11/3,AB/7 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10253732 BIOSIS NO.: 199698708650
A cyclic nucleotide suppressible conductance is the target of the transducin-PDE-based taste **transduction cascade.**
AUTHOR: Kolesnikov Stanislav(a); **Margolskee Robert F**
AUTHOR ADDRESS: (a)Inst. Cell Biophysics, Russian Academy Science Puschino, Moscow Region 142292**Russia
JOURNAL: Chemical Senses 20 (6):p723 1995
CONFERENCE/MEETING: Seventeenth Annual Meeting of the Association for Chemoreception Sciences (AChemS XVII) Sarasota, Florida, USA April 1995
ISSN: 0379-864X
RECORD TYPE: Citation
LANGUAGE: English
1995

11/3,AB/8 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10074828 BIOSIS NO.: 199598529746
Characterization of bitter **receptors that activate alpha-gustducin and transducin in** taste **membranes.**
AUTHOR: Ruiz-Avila L; **Margolskee R F**
AUTHOR ADDRESS: Roche Inst. Molecular Biology, 340 Kingsland Street, Nutley, NJ 07110**USA
JOURNAL: Society for Neuroscience Abstracts 21 (1-3):p1657 1995
CONFERENCE/MEETING: 25th Annual Meeting of the Society for Neuroscience San Diego, California, USA November 11-16, 1995
ISSN: 0190-5295
RECORD TYPE: Citation
LANGUAGE: English
1995

11/3,AB/9 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08904771 Genuine Article#: 343JY Number of References: 71
Title: The molecular physiology of taste **transduction** (ABSTRACT AVAILABLE)
Author(s): Gilbertson TA (REPRINT) ; Damak S; **Margolskee RF**
Corporate Source: UTAH STATE UNIV,DEPT BIOL, 5305 OLD MAIN HILL/LOGAN//UT/84322 (REPRINT); CUNY MT SINAI SCH MED,DEPT PHYSIOL & BIOPHYS, HOWARD HUGHES MED INST/NEW YORK//NY/10029
Journal: CURRENT OPINION IN NEUROBIOLOGY, 2000, V10, N4 (AUG), P519-527
ISSN: 0959-4388 Publication date: 20000800
Publisher: CURRENT BIOLOGY LTD, 84 THEOBALDS RD, LONDON WC1X 8RR, ENGLAND
Language: English Document Type: REVIEW
Abstract: **Taste** receptor cells use a variety of mechanisms to transduce chemical information into cellular signals. Seven-transmembrane-helix receptors initiate signaling cascades by coupling to G proteins, effector enzymes, second messengers and ion channels. Apical ion channels pass ions, leading to depolarizing and/or hyperpolarizing responses. New insights into the mechanisms of **taste** sensation have been gained from molecular cloning of the transduction elements, biochemical elucidation of the transduction pathways, and electrophysiological analysis of the function of **taste** cell ion channels.

11/3,AB/10 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05192056 Genuine Article#: VG349 Number of References: 76
Title: MECHANISMS OF TASTE **TRANSDUCTION** (Abstract Available)
Author(s): KINNAMON SC; **MARGOLSKEE RF**
Corporate Source: COLORADO STATE UNIV,DEPT ANAT & NEUROBIOL/FT COLLINS//CO/80523; UNIV COLORADO,HLTH SCI CTR,ROCKY MT TASTE & SMELL CTR/DENVER//CO/80262; MT SINAI SCH MED,DEPT PHYSIOL & BIOPHYS/NEW YORK//NY/00000
Journal: CURRENT OPINION IN NEUROBIOLOGY, 1996, V6, N4 (AUG), P506-513
ISSN: 0959-4388
Language: ENGLISH Document Type: ARTICLE
Abstract: **Taste** cells use a wide variety of mechanisms for transduction. Ionic stimuli, such as salts and acids, interact directly with ion channels to depolarize **taste** cells. More complex stimuli, such as sugars and amino acids, utilize apically located receptors for transduction. Recent molecular biological results suggest that the metabotropic glutamate receptor mGluR4, may function in glutamate **taste** transduction, New biochemical studies have identified a **bitter** -responsive receptor that activates gustducin. Unexpected results with knockout mice suggest that gustducin may be directly involved in both

bitter and sweet transduction. Electrophysiological experiments indicate that both inositol trisphosphate and cyclic nucleotides function in both **bitter** and sweet transduction events.

11/3,AB/11 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04116588 Genuine Article#: RH111 Number of References: 28
Title: A CYCLIC-NUCLEOTIDE-SUPPRESSIBLE CONDUCTANCE ACTIVATED BY TRANSDUCIN IN TASTE **CELLS** (Abstract Available)
Author(s): KOLESNIKOV SS; **MARGOLSKEE RF**
Corporate Source: ROCHE INST MOLEC BIOL,ROCHE RES CTR/NUTLEY//NJ/07110; ROCHE INST MOLEC BIOL,ROCHE RES CTR/NUTLEY//NJ/07110; RUSSIAN ACAD SCI,INST CELL BIOPHYS/PUSHCHINO 142292//RUSSIA/
Journal: NATURE, 1995, V376, N6535 (JUL 6), P85-88
ISSN: 0028-0836
Language: ENGLISH Document Type: ARTICLE
Abstract: **TASTE** can be divided into four primary sensations: salty, sour, sweet and **bitter** , Salty and sour are directly transduced by apical channels(1-4), whereas sweet and **bitter** utilize cyclic nucleotide second messengers(5-11). We have shown that rod transducin is present in mammalian **taste** receptor cells, where it is activated by a **bitter** receptor and in turn activates a phosphodiesterase(12). Here we introduce into frog **taste** cells peptides derived from transducin's phosphodiesterase-interaction region, which cause an inward whole-cell current in a subset of cells, We find that the peptides' effects are reversibly suppressed by IBMX and forskolin, indicative of a transducin-activated phosphodiesterase. Cyclic nucleotides suppress the whole-cell current, indicating that cyclic nucleotides may regulate **taste** -cell conductance. IBMX modifies **taste** -cell responses to two **taste** stimuli, implicating phosphodiesterase in **taste** transduction. Submicromolar cyclic nucleotides directly suppress the conductance of inside-out patches derived from the **taste** -cell plasma membrane, independently of protein phosphorylation. The channels are unusual in that they are suppressed, rather than activated by cyclic nucleotides, We propose that transducin, via phosphodiesterase, decreases cyclic nucleotide levels to activate the cyclic-nucleotide-suppressible conductance, leading to Ca2+ influx and **taste** -cell depolarization.
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Abstract View

FUNCTIONAL EXPRESSION OF TRP-T, A STORE OPERATED CALCIUM CHANNEL EXPRESSED IN TASTE CELLS

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3. University of California, Irvine, CA, USA

Taste receptor cells (TRCs) transduce responses to tastants using a diversity of mechanisms including ion channels (for sodium salts, acids, and fat taste) and G-protein coupled receptor (GPCR) cascades (for sugars, sweeteners, bitter and glutamate/umami compounds). During the past decade, a number of constituent elements from these GPCR cascades have been identified. Among those elements there are the T2R/TRB family of candidate receptors for bitter compounds, T1R3, a candidate receptor for sweet compounds, the G protein subunits α-gustducin, Gβ3 and Gγ13, and downstream elements such as PDE1A, PLCβ2, and IP3 type III receptor (IP3R3). Nevertheless, additional downstream elements are expected to be present in TRCs. To better understand the transduction pathways in gustducin-positive TRCs we set out to identify genes preferentially expressed in gustducin-positive TRCs. Differential hybridization screenings led us to the cloning of TRP-T, a novel member of the Trp (transient receptor potential) family of ion channels. TRP-T co-expresses with α-gustducin, Gβ3, Gγ13, PLCβ2 and IP3R3 in TRCs. Functional expression of TRP-T studied by electrophysiological and calcium imaging techniques demonstrated its ability to work as a store operated calcium channel, sensitive to inhibition by lanthanum. TRP-T is a putative effector present in the sweet and bitter transduction pathways of TRCs.

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